General

Guideline Title

Clinical practice guideline for the management of patients with Parkinson's disease.

Bibliographic Source(s)

Working Group of the Clinical Practice Guideline for the Management of Patients with [trunc]. Clinical practice guideline for the management of patients with Parkinsonâ€™s disease. Madrid (Spain): Ministry of Health, Social Services and Equality; Institute of Health Sciences of Aragon; 2014. 159 p. [124 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Levels of evidence (1++ to 4) and grades of recommendation (A to D, GCP) are defined at the end of the "Major Recommendations" field.

Pharmacological Treatment

Motor Symptoms

Antiparkinson Drugs

Question to Be Answered: Is non-oral administration of antiparkinson treatments (dopaminergics and anticholinergics) used for motor symptoms safer and more effective?

B - The use of levodopa/carbidopa intestinal gel (LCIG) is recommended only for the treatment of advanced Parkinson's disease (PD) with severe motor fluctuations and hyper/dyskinesia when the available combinations of the Parkinson's medications have not produced satisfactory results. This alternative may be cost effective with the conditions established within the framework of usage of orphan drugs.

B - Evaluation of antiparkinson treatment with transdermal rotigotine is recommended for patients with early or initial PD, at the doses specified in the product sheet, when other alternatives are ineffective.

B - Intermittent injections of apomorphine may be used to reduce motor fluctuations (*"on-off"* phenomena) in patients with PD in which symptoms are not controlled sufficiently by oral antiparkinson medication.

D - Continuous subcutaneous infusions of apomorphine may be used to reduce *off* time and dyskinesia in persons with PD and severe motor

complications. This should only be initiated in expert units with facilities to allow adequate supervision.

Management of Problems Related to Antiparkinson Medications

Drug-induced Psychosis

Question to Be Answered: Is it more effective and safer to add an atypical antipsychotic (for example: quetiapine) to antiparkinson medication or reduce/discontinue these antiparkinson drugs (anticholinergics, selegiline, amantadine) to control the drug-induced psychosis associated with this disease?

D - All persons with PD and psychosis should receive a general medical evaluation, in order to exclude other treatable causes of psychosis.

D - Before considering the use of anti-psychotic medication, treatment for any precipitant condition is recommended.

D - The gradual discontinuation of antiparkinson medication that could trigger psychosis in persons with PD must be taken into account.

D - It may not be necessary to treat moderate psychotic symptoms in persons with PD if they are tolerated well by the patient and the caregiver.

D - Typical antipsychotics (such as phenothiazines and butyrophenones) should not be used in persons with PD because they may exacerbate the motor characteristics of PD.

D - Atypical antipsychotics may be considered for treatment of psychotic symptoms in persons with PD, although the evidence of its efficacy and safety is limited.

A - The use of clozapine at the minimum effective dose is indicated in patients who develop psychotic disorders over the course of their PD, in cases in which standard treatment has failed.

D - When treatment with clozapine is applied, weekly monitoring is recommended during the first 18 weeks of treatment, followed by monitoring for as long as the treatment is continued (at least once every 4 weeks). These analytical controls should be continued for 4 weeks after complete interruption of the treatment.

D - Treatment of psychotic symptoms in patients with PD with clozapine requires the mandatory registration of the monitoring scenario of the atypical antipsychotic and of blood parameters (total white blood cell count and absolute neutrophil count). For more information, see the product sheet (http://www.aemps.gob.es/).

B - The use of low doses of quetiapine may be considered as an alternative antipsychotic to clozapine for the treatment of patients with psychosis in PD, when weekly routine blood monitoring is not possible, and within the framework of Royal Decree 1015/2009, dated 19 June, regulating the availability of medications in special situations.

Sleep Disorders

Question to Be Answered: Which treatment is safest and most effective to reduce the sleep disorders associated with PD?

D - The treatment of excessive daytime sleepiness (EDS) must be aimed at finding a reversible cause, such as depression, poor sleep hygiene, or medications, associated with the altered sleep pattern.

D - Modafinil and melatonin are not recommended for the management of EDS associated with PD.

D - Modified-release levodopa products may be used for nocturnal akinesia in patients with PD.

D - The sleep history of the patients with PD should be recorded to document the sleep disorder.

D - Proper sleep hygiene is recommended for persons with PD and any sleep disorder, including:

- Avoid intake of stimulants in the afternoon (e.g., coffee, tea, etc.)
- Establish a regular sleep pattern
- Comfortable bedroom temperature and setting
- Provide healthcare products, such as bed lifts or rails to assist with movement and turning, which helps make people more comfortable
- Restrict naps during the day
- Recommend regular and adequate exercise to sleep better
- Review all of the medication and avoid drugs that affect sleep or alertness, or that could interact with other medication (e.g., selegiline, antihistamines, H2 antagonists, antipsychotics, and sedatives)

D - Special care should be taken to identify and control sleep behaviour disorders, such as restless leg syndrome and the REM (rapid eye movement) phase in persons with PD and sleep disorders.

D - Persons with PD who have sleep attacks should be advised not to drive or expose themselves to occupational risks. An attempt should be made to adjust medication in order to reduce the occurrence of these attacks.

GCP - Patients should be advised to exercise caution with medication that could alter their ability to drive or operate machinery, and should read the information available on the packaging of this medication: the warning symbol or pictogram on the box (driving pictogram), which is supplemented by the information provided in the prospectus.

GCP - Persons with PD are recommended to maintain proper sleep hygiene, by doing physical exercise at least a few hours before going to sleep and using satin sheets to facilitate turning in bed.

Impulse Control Disorders

Question to Be Answered: Which treatment is safest and most effective in controlling the impulse control disorders associated with the treatment of PD using dopamine agonists?

B - The management of impulse control disorders (ICD) in patients with PD should include the consideration of the reduction or discontinuation of the use of dopamine agonists, using a selective serotonin uptake inhibitor (SSRI), and probably psycho-social counseling and support.

B - Ergoline dopamine agonists should not be used as the first line of treatment of PD and ICD.

A - Switching between dopamine agonists in patients with PD and ICD is not recommended.

D - When ergoline dopamine agonists are used, patients should follow:

- A baseline screening echocardiography and regular follow-up scans to identify cardiac abnormalities
- Baseline laboratory investigation (e.g., erythrocyte sedimentation rate, serum creatinine) and radiological investigation (chest x-ray) with regular follow-up monitoring to identify serosal fibrosis

A - Patients should be warned of the potential of dopamine agonists to cause ICD and EDS, and should be informed of the effects on driving and management of machinery.

B - Special attention should be given to detect signs of ICD in young male patients with PD and a prior history of behavioural disorders or addictive behaviour.

GCP - Healthcare workers should discuss the possible complications of ICD with the patients with PD who are taking dopamine agonists.

Cognitive Impairment

Question to Be Answered: In adults with PD who develop initial cognitive impairment, is it safer and more effective to add an acetylcholinesterase inhibitor, or modify dopaminergic treatment to improve cognitive functioning symptoms?

A - The use of the acetylcholinesterase inhibitor rivastigmine in patients with idiopathic PD who present with mild to moderately severe dementia is recommended.

GCP - The evaluation of different intervention strategies, including cognitive stimulation is recommended to treat patients with PD who present with initial mild cognitive deterioration, before establishing specific pharmacological treatment with rivastigmine.

D - In patients with PD and cognitive impairment, the causes of dementia should be investigated, and if present, they should be treated.

D - The exclusion of any other non-Parkinson medication that acts on the central nervous system should be considered, with the discontinuation of anticholinergic medication, amantadine, selegiline, and dopamine agonists.

GCP - A systematic review of the treatments prescribed for the management of the motor symptoms of PD is recommended, evaluating the indication, adherence, and interactions, in order to reduce the risk of adverse side-effects such as cognitive impairment, to reduce polypharmacy and agree upon treatments with the patient.

Non-motor Symptoms

Sensory Symptoms

Question to Be Answered: Which treatment is safest and most effective in controlling the alterations with sensory symptoms associated with PD? (e.g., visual alterations; olfactory dysfunction; taste alterations; hypoacusis and other auditory disorders; pain and associated sensitivity symptoms).

GCP - It is advisable to inform patients of the possible alterations with sensory symptoms associated with PD, in order to work on them as a team (patients, family members, and caregivers, along with the healthcare professionals) and reduce the impact of those alterations on the lives of the people affected by this disease.

Autonomic Dysfunctions

Question to Be Answered: Which treatments are safest and most effective in controlling the autonomic dysfunctions associated with PD? (e.g., orthostatic hypotension; constipation; fecal incontinence; nausea and vomiting; hypersalivation; intolerance to heat; excessive sweating; nocturia; sexual dysfunction; weight loss; difficulty swallowing).

GCP - Patients with PD should be advised to avoid the precipitating factors of orthostatic hypotension, such as sudden changes in posture, large meals, hot baths, and vasodilation medication.

GCP - Managing orthostatic hypotension in patients with PD is recommended, using non-pharmacological measures before initiating pharmacological treatment. Non-pharmacological measures include avoiding meals that are low in sodium and high in carbohydrates, increasing intake of water (2-2.5 l/d) and salt (>8 g or 150 mmol/d) in the diet, breaking up meals, exercise, elevating the head while sleeping, wearing compression stockings, or carrying out physical containment movements to increase blood pressure by increasing venous return and peripheral resistance, such as squatting, leaning forward, or crossing legs at the onset of presyncopal symptoms. Get out of bed slowly and stay seated in bed for a few seconds before standing.

GCP - It is advisable to reconsider treatments that induce or aggravate orthostatic hypotension in patients with PD, including the review of all medications, taken with or without a prescription, and other products that could cause hypotension.

D - Persons with PD must be properly treated for the autonomic disorder that results in urinary dysfunction, weight loss, dysphagia, constipation, orthostatic hypotension, excessive sweating, and sialorrhea.

GCP - It is advisable to consider the discontinuation of medication that could induce sialorrhea, such as cholinesterase inhibitors, clozapine, or quetiapine.

B - Patients should be advised that treatments that could potentially produce sexual dysfunction (e.g., treatments for hypertension and depression) should be re-evaluated.

B - The use of sildenafil is not recommended for patients with PD and sexual dysfunction.

B - The evaluation of other comorbidities that could result in erectile dysfunction is recommended, such as depression or concurrent sexual dysfunction, especially low sex drive, as well as the deficiency of sex hormones, because the PD may not be the principal cause of the sexual dysfunction.

GCP - The evaluation of possible causes of urinary dysfunction in patients with PD, such as prostate hypertrophy or cancer, is recommended.

GCP - Changes in diet and physical activity are recommended for patients with PD and constipation. Increase intake of liquids and fibre, with fibre supplements and stool softeners, if necessary.

GCP - It is advisable to consider and evaluate treatments that frequently cause constipation (tricyclic depressants, loperamide, codeine and opioids, antimuscarinics, and some antiparkinson drugs).

GCP - The preparation of an exhaustive pharmacotherapeutic sheet is recommended for patients with PD, in order to determine medications and products that could potentially interact with each other.

B - Domperidone is recommended for problems of gastrointestinal motility (anorexia, nausea, vomiting) associated with treatment with levodopa and dopamine agonists).

GCP - The use of metoclopramide is not recommended in patients with PD due to the aggravation of the motor symptoms.

Depression as Associated Comorbidity

Question to Be Answered: Are selective serotonin reuptake inhibitors (SSRIs) safer and more effective than tricyclic antidepressants (TCAs) for controlling depression associated with PD?

D - The management of depression in persons with PD should be personalized, specifically taking into account concurrent treatments and any comorbidities that are present.

GCP - The selection of the treatment for depression will depend on the prior experience of the healthcare professional and the clinical condition of the patient.

B - Based on the comorbidities presented by the person affected by PD, tricyclic antidepressants may be chosen as a short-term treatment.

GCP - The evaluation of other non-pharmacological alternatives is recommended for the treatment of depression in persons with PD, such as psychotherapy.

GCP - A multi-discipline approach is recommended for the management of severe depression associated with PD.

Non-pharmacological Treatment

Occupational and Physical Therapy

Question to Be Answered: How effective is physical therapy in persons with PD?

A - Offering persons newly affected by PD rehabilitation treatment based on physical therapy is recommended.

B - It would be advisable to include physical therapy techniques as part of the interdisciplinary approach to PD, placing special emphasis on the functional rehabilitation of the patient.

A - The use of exercise programmes for strengthening/stretching/functioning, supervised aerobic exercise, low-intensity treadmill running, and progressive endurance exercises are recommended in patients with PD.

GCP - There are other complementary techniques for patients with PD, which can be evaluated based on the characteristics of the patients and their environment, such as tai-chi, training with video games that involve physical exercise and dance.

B - Physical therapy must be available to persons with PD throughout the process of the disease. Special attention should be given to:

- Re-education of walking, with improvement of balance and flexibility
- Strengthen aerobic capacity
- Improve initiation of movement
- Improve functional independence, including mobility and activities of daily life
- Give advice in regard to safety in the home

C - The Alexander technique can benefit persons with PD by helping them to make lifestyle adjustments that affect both the physical nature of the condition, as well as the attitudes of the person who has PD.

Question to Be Answered: How effective is occupational therapy in improving functional independence in persons with PD?

D - Occupational therapy must be available for persons with PD. Special attention should be given to:

- Maintaining jobs and family roles, instrumental and advanced daily life, domestic, and leisure activities
- Improving and maintaining movement and mobility
- Improving personal care activities such as eating, drinking, washing, and dressing
- The aspects of the environment to improve safety and motor functions
- Cognitive evaluation and appropriate intervention

B - In patients mildly affected by PD, occupational therapy is recommended in order to improve the perceived functional capacity for the activities of daily life of these persons.

Speech Therapy

Communication and Language

Question to Be Answered: How effective is speech therapy in improving communication and language in persons with PD?

D - Speech therapy should be made available to persons with PD. Special attention should be given to:

- Improvement of voice volume and tone range, including speech therapy programs such as LSVT (speech therapy using the Lee Silverman

Voice Treatment technique)
- Teaching strategies to optimize intelligibility of language
- Guarantee that the effective instruments of communication are maintained over the course of the disease, including the use of assisting technologies
- Review and manage to support the safety and effectiveness of chewing and to minimize the risk of choking

GCP - Evaluation of the use of the LSVT technique and the evaluation of the results of patients with PD affected by speech and language disorders, especially in the most clinically relevant variable, intelligibility of speech, is recommended.

Swallowing

Question to Be Answered: How effective is speech therapy in improving swallowing in persons with PD?

GCP - Evaluation of the use of the LSVT technique for managing swallowing difficulties in persons with PD is recommended.

B - Evaluation of the use of video-assisted swallowing therapy (VAST) to improve swallowing in persons with PD is recommended.

GCP - The use of the chin-tuck technique together with thin liquids to reduce the incidence of pneumonia as a result of aspiration should not be considered as the first line of action in patients with PD and swallowing disorders.

GCP - A multi-discipline approach is recommended to manage swallowing disorders in persons affected by PD. It would be especially advisable to form coordinated work teams that include healthcare professionals specialized in endocrinology and nutrition, physical medicine and rehabilitation, hospital pharmacy, as well as speech therapists, dieticians-nutritionists, nurses, and occupational therapists, in order to promote the synergy among the tasks of rehabilitation, education, and nutritional support.

Neuropsychology

Question to Be Answered: How effective is rehabilitation of cognitive functions in persons with PD?

GCP - It is advisable to carry out neuropsychological evaluations of patients with PD in order to document baseline cognitive state and track its evolution.

GCP - Facilitating the improvement of cognitive functions in patients with PD using tools developed by multi-discipline teams is recommended.

Nutrition and Diet

Vitamin D Supplementation

Question to Be Answered: How effective and safe is supplementation with vitamin D for the prevention of falls and hip fractures in persons with PD who present with a lack of renal synthesis of 1.25-dihydroxyvitamin D?

B - Supplementation with vitamin D (as part of the diet, through enriched foods, food supplements, or medication) helps to prevent fractures in patients with PD who do not ingest a sufficient quantity, or who have a deficit of exposure to sunlight or have a greater need for vitamin D.

GCP - If an additional supplement of vitamin D is required in persons with PD, the association of calcium is recommended, provided that the patient does physical exercise or the daily calcium requirements are not covered by diet.

GCP - Food supplements should not be used as a substitute for a balanced diet in persons with PD and adequate nutrition and sufficient exposure to sunlight.

Weight Loss

Question to Be Answered: How effective are the different treatments aimed at weight loss in the treatment of obese and overweight persons with PD?

GCP - Persons affected by PD and who are overweight or obese are recommended to exercise moderately, receive a healthy diet, and develop a lifestyle that helps reduce the impact of this chronic disease and its associated comorbidities.

Modification of Protein Intake

Question to Be Answered: What is the effect of the modification of protein intake in the necessary dose of levodopa in persons recently diagnosed with Parkinson's and in persons with PD?

GCP - It may be advisable to inform patients to keep protein intake within the recommended dietary requirements (≈0.8 g/kg/day) when beginning treatment with levodopa. Routine dietary evaluation to ensure compliance is recommended.

GCP - The participation of healthcare professionals specialized in human nutrition and diet as part of the multi-discipline teams may help to achieve and maintain compliance in regard to the recommended daily protein intake.

GCP - Although there is no conclusive evidence, when motor fluctuations occur and drug-nutrient interaction is suspected, a diet with redistribution of proteins may be proposed to patients with PD who are mentally active, motivated, and highly cooperative, but the possible side effects must be considered and managed.

Definitions

Scottish Intercollegiate Guidelines Network (SIGN) Levels of Evidence

1++	High-quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of clinical trials, or well-conducted clinical trials with low risk of bias
1-	Meta-analyses, systematic reviews of clinical trials or clinical trials with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies. High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2-	Cohort or case-control studies with high risk of bias and a significant risk that the relationship is not causal
3	Non-analytic studies, such as case reports and case series
4	Expert opinion

Note: Studies classified as 1- and 2- should not be used for making recommendations due to their high potential for bias.

SIGN Grades of Recommendation

A	At least one meta-analysis, systematic review or clinical trial rated as 1++ and directly applicable to the target population of the guide; or a body of evidence consisting of studies rated as 1+ and showing overall consistency of results
B	A body of evidence consisting of studies rated as 2++, directly applicable to the target population of the guide and showing overall consistency of results; or evidence extrapolated from studies rated as 1++ or 1+
C	A body of evidence consisting of studies rated as 2+ directly applicable to the target population of the guide and showing overall consistency of results; or evidence extrapolated from studies rated as 2++
D	Evidence levels 3 or 4; or evidence extrapolated from studies rated as 2+
Good Clinical Practice (GCP)*	Recommended practice based on clinical experience and consensus of the editorial team

*Sometimes the development group wishes to highlight an important practical aspect for which there is probably no supporting evidence. In general, these cases are related to an aspect of treatment generally accepted to be good clinical practice, and are evaluated as a point of good clinical practice. These messages are not an alternative to the evidence-based recommendations, but should be considered only when there is no other way of highlighting that aspect.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Parkinson's disease (PD)

Note: Secondary Parkinson's, which covers Parkinson's induced by neuroleptics and drug-induced Parkinson's is excluded. Other types of dementia that are similar to Parkinson's that are covered in the clinical practice guidelines (CPG) on the comprehensive care of persons with Alzheimer's disease and other dementia, such as dementia with Parkinson's or dementia with Lewy bodies are also excluded.

Guideline Category

Management

Rehabilitation

Treatment

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Neurological Surgery

Neurology

Nursing

Nutrition

Pharmacology

Physical Medicine and Rehabilitation

Psychiatry

Psychology

Sleep Medicine

Speech-Language Pathology

Intended Users

Advanced Practice Nurses

Dietitians

Health Care Providers

Nurses

Occupational Therapists

Physical Therapists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Social Workers

Speech-Language Pathologists

Guideline Objective(s)

To provide healthcare professionals and persons affected by Parkinson's disease (PD) with recommendations based on the best available scientific evidence to facilitate decision-making in the clinical management of the disease

Target Population

Adults with Parkinson's disease (PD) in any stage, of any age or gender, without restricting the presence of pluripathology or comorbidities

Note: Individuals with secondary PD, which covers Parkinson's induced by neuroleptics and other drugs, are outside the scope of this guideline. Individuals with other types of dementia (e.g., Alzheimer's disease) are also excluded.

Interventions and Practices Considered

1. Pharmacological treatment of motor symptoms
    - Levodopa/carbidopa intestinal gel (LCIG)
    - Transdermal rotigotine
    - Intermittent injections of apomorphine
    - Continuous infusion of apomorphine
2. Management of drug-induced psychosis
    - Atypical antipsychotics (e.g., quetiapine)
    - Gradual discontinuation of antiparkinson drugs
    - Clozapine
3. Management of sleep disorders
    - Modified-release levodopa products
    - Proper sleep hygiene
    - Avoiding stimulants
4. Management of impulse control disorders
    - Reduction or discontinuation of dopamine agonists
    - Selective serotonin uptake inhibitors (SSRIs)
    - Psychosocial counseling and support
    - Ergoline dopamine agonists (not recommended as first-line therapy)
    - Monitoring for complications
5. Management of cognitive impairment
    - Acetylcholinesterase inhibitors (e.g., rivastigmine)
    - Evaluation of different intervention strategies, including cognitive stimulation activities
    - Determination of cause
    - Discontinuation of anticholinergic medication, amantadine, selegiline, and dopamine agonists
6. Counseling and advice on management of sensory symptoms
7. Evaluation and management of autonomic dysfunctions (e.g., orthostatic hypotension, constipation, fecal incontinence, nausea and vomiting, hypersalivation, intolerance to heat, excessive sweating, nocturia, sexual dysfunction, weight loss, difficulty swallowing)
    - Avoiding precipitating factors
    - Re-evaluation or discontinuation of medications
    - Domperidone for problems of gastrointestinal motility
8. Management of depression
    - Tricyclic antidepressants
    - Individualized treatment
    - Nonpharmacological alternatives such as psychotherapy

9. Physical therapy
10. Occupational therapy
11. Speech therapy
    - Communication and language therapy (e.g., Lee Silverman Voice Treatment [LSVT] technique)
    - Swallowing therapy (e.g., LSVT, video-assisted swallowing therapy)
12. Neuropsychological evaluation
13. Nutrition and diet
    - Vitamin D supplementation
    - Weight loss for treatment of obesity and overweight
    - Modification of protein intake

Note: The following were considered but not recommended: typical antipsychotics, sildenafil, metoclopramide, modafinil and melatonin.

Major Outcomes Considered

- Control of motor and non-motor symptoms
- Activities of daily life
- Safety of antiparkinson medication
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Clinical questions were formulated following the PICO format (Patient/Intervention/Comparison/Outcome).

Bibliographic search was carried out in databases and other specialised sources: Medline (through PubMed), EMBASE (Elsevier), The Cochrane Library, Centre for Reviews and Dissemination (CRD) of the University of York (includes the DARE databases [Database of Abstracts of Reviews of Effects], NHS EED [National Health Service Economic Evaluation Database], and HTA [Health Technology Assessment]), Índice Bibliográfico Español en Ciencias de la Salud (IBECS) and Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS). For the question regarding occupational therapy, a search was done in the specialised database OTseeker, and for the question regarding physical therapy, the Physiotherapy Evidence Database (PEDro) was consulted.

Languages: English and Spanish. Search period 10 years (2003 to 2013). Trial type filters: systematic reviews (SRs), clinical practice guidelines (CPGs), and randomized controlled trials (RCTs).

The search strategies, accessible as additional material (see the "Availability of Companion Documents" field), were carried out combining terms in controlled language for each database (MeSH, Emtree, DeCS) and free language. In the initial phase, a preliminary search was made of CPGs and systematic reviews in the aforementioned databases. These were included as a secondary source of CPG evidence, to respond to specific sections of the guidelines, in accordance with the methodology proposed in the asthma guidelines of the Basque Country.

The guidelines included were evaluated using the instrument AGREE II (Appraisal of Guidelines Research and Evaluation). The methodological material of the guidelines presents the scores obtained after applying the instrument AGREE II to two CPGs on Parkinson's disease (PD) consulted during the preparation of the guidelines (National Institute for Health and Care Excellence [NICE], 2006, and Scottish Intercollegiate

Guidelines Network [SIGN], 2010).

The minimum requirement established to constitute a source of evidence for this guideline was a score, using the AGREE Instrument, higher than 60% in domains 1, 3, and 6. The level of evidence established for the RCTs and SRs specified in the CPGs was maintained. In the second phase, an expanded search of original trials (mainly RCTs) was done, and for some questions, www.clinicaltrials.gov was also consulted. A reverse search was done in the references of the articles identified and included in the CPGs. The authors of the studies were contacted directly when necessary. In addition, automatic e-mail alerts were defined for new studies included in Medline, EMBASE, and The Cochrane Library.

The search reports were evaluated by at least two members of the guideline working group (GWG). The screening was done initially by title and summary. In a second screening, the discarded studies were recorded and the causes for exclusion were specified. The studies that were finally selected were evaluated using the critical reading tool of the Agency for Healthcare Technology Assessment of the Basque Country - OSTEBA.

For the question regarding the efficacy of physical therapy in persons with PD, general physical therapy was evaluated, and a non-systematic review was done for other techniques, such as music and dance, martial arts or tai-chi, among others.

Number of Source Documents

Refer to the Methodological Material document (see the "Availability of Companion Documents" field) for a breakdown of the identified studies and included studies for each clinical question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Scottish Intercollegiate Guidelines Network (SIGN) Levels of Evidence

1++	High-quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with very low risk of bias
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3	Non-analytic studies, such as case reports and case series
4	Expert opinion

Note: Studies classified as 1- and 2- should not be used for making recommendations due to their high potential for bias.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The studies that were finally selected were evaluated using the critical reading tool of the Agency for Healthcare Technology Assessment of the

Basque Country - OSTEBA. These studies were classified according to the evidence levels proposed by Scottish Intercollegiate Guidelines Network (SIGN) (see the "Rating Scheme for the Strength of the Evidence" field).

The detailed information on the methodology applied to the clinical practice guideline (CPG) (search strategies for each clinical question and tables summarizing the evidence and formal evaluation) are available from GuíaSalud Web site (see also the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The methodology used in the preparation of this clinical practice guideline (CPG) is set out in the *Methodology Manual for Preparation of CPG in the National Health System (NHS)*.

The development of this CPG began with the creation of the Guideline Working Group (GWG), made up of primary-care and specialised professionals (medicine, pharmacy, nursing), specialists in neurology, psychiatry, physical therapists, speech therapists, dieticians-nutritionists for home hospitalization. The GWG did not include patients, family members, or caregivers; the Director General of the Spanish Parkinson's Federation was consulted as a collaborating expert. Potential users of the information aimed at patients were also consulted in the review of this content.

Formulation of recommendations was based on the "formal evaluation" or "justified opinion" of Scottish Intercollegiate Guidelines Network (SIGN). The classification of the evidence and the grading of the recommendations were done using the SIGN system. Recommendations that were controversial or that lacked evidence were resolved by consensus in a meeting of the working group. The collaborating experts participated in the formulation of questions and the revision of the first draft of the guidelines.

Rating Scheme for the Strength of the Recommendations

Scottish Intercollegiate Guidelines Network (SIGN) Grades of Recommendation

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Cost Analysis

- Results of one economic evaluation showed that levodopa-carbidopa intestinal gel (LCIG) as an orphan drug can be considered to be cost-effective in the context of the United Kingdom.
- The results of a cost-utility analysis (CUA) for LCIG are above the maximum values of cost-effectiveness and willingness to pay (WTP).
- Rivastigmine can improve care in patients who have developed mild to moderate dementia at least two years after receiving the clinical diagnosis of Parkinson's disease (PD). A small improvement was observed in the quality-adjusted life years. No cost differences were

observed.
- Physical therapy is relatively inexpensive and is therefore probably cost-effective if a small improvement in health can be demonstrated. Study results support the cost-effectiveness of intervention with exercises aimed at reducing falls, but are not statistically significant enough to establish a definitive conclusion.

See the original guideline document for more information on cost-effectiveness analyses reviewed for this guideline.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

External reviewers participated in the revision of the second draft. The different scientific societies involved were contacted: Spanish Association of Physical Therapists (AEF), Spanish Association of Speech Therapy and Audiology (AELFA), Spanish Association of Neuropsychiatry (AEN), Spanish Professional Association of Occupational Therapists (APETO), Federation of Associations of Community Nursing and Primary Care (FAECAP), Spanish Parkinson's Federation (FEP), Spanish Foundation of Dieticians and Nutritionists (FEDN), Spanish Society of Primary Care Pharmacists (SEFAP), Spanish Society of Family and Community Medicine (SemFYC), Spanish Society of General and Family Physicians (SEMG), Spanish Society of Primary Care Physicians (SEMERGEN), Spanish Neurology Association (SEN), Spanish Society of Psychiatry (SEP), Spanish Society of Biological Psychiatry (SEPB), Spanish Society of Rehabilitation and Physical Medicine (SERMEF), which are also represented by the members of the working group, the collaborating experts, and external reviewers.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with Parkinson's disease resulting in reduced disease symptoms, improved activities of daily life, and reduced side effects of antiparkinson medication

Refer to the original guideline document for information about the benefits of specific interventions observed in the studies that were reviewed for this guideline.

Potential Harms

- The effectiveness of levodopa decreases over time. It has been calculated that five years after initiating treatment, a high percentage of patients develop what are known as motor fluctuations, characterised by the alternation of *"on"* periods and *"off"* periods. Over the years, these fluctuations may become more pronounced, which means that the periods of time during which the medication is ineffective become longer and less predictable. This is when the side effects caused by the levodopa appear: mental disorders, increased sex drive, lower blood pressure, digestive alterations. In addition, administration of levodopa over an extended period of time may facilitate the appearance of excessive abnormal involuntary movements that cannot be controlled by the patient.
- Some of the frequent adverse reactions to transdermal rotigotine include: sleep attacks/sudden sleep episodes, insomnia, sleep disorders, abnormal dreams, among others.

- Anticholinergics are indicated only in very specific cases and in patients younger than 70 years of age, due to the side effects, which include blurry vision, urine retention, and memory loss.
- Care must be taken when prescribing subcutaneous apomorphine because it could easily worsen pre-existing psychiatric symptoms. Nodes may appear at the point of subcutaneous injection. Other adverse events include: nausea, dyskinesia, recurring diarrhoea, confusion, mood swings, orthostatic hypotension, short-duration trembling of the legs, sweating and hot flashes, drowsiness, vertigo, eosinophilia, or lowered motor functioning at the end of the clinical effect compared with the basic level before the test, etc.
- Selegiline may have more side effects than rasagiline, including insomnia and hallucinations.
- There are two possible problems with the use of antidepressants to treat depression in patients with PD. These are the possibility of extrapyramidal symptoms (such as dystonia, akathisia, tremors, and parkinsonism), and the possibility of an adverse interaction with selegiline, an monoamine oxidase B (MAO B) inhibitor sometimes used in the treatment of PD. Although the use of SSRIs in PD with or without selegiline appears to be safe, caution is recommended when introducing these drugs.
- Clozapine has been associated with agranulocytosis, so regular monitoring of the total white blood cell count and the absolute neutrophil count is necessary for patients who are treated with this medication. In patients treated with clozapine, a significant increase in average resting heart rate, body weight, and drowsiness was reported. Treatment of psychotic symptoms in patients with PD with clozapine requires the mandatory registration of the monitoring scenario of the atypical anti-psychotic and of blood parameters.
- Ergoline and non-ergoline dopamine agonists are associated with an increased risk of impulse control disorders (ICDs) which include ludopathy, binge eating, and hypersexuality.
- The following adverse effects were observed during exercises: discomfort or muscle pain, falls, wrist pain, dizziness or fainting.
- With the protein-redistribution diet, the following complications or side effects were detected: severe dyskinesia (which led to a reduction of the levodopa dose), moderate weight loss, and hunger before dinner.

Refer to the original guideline document for information about the harms of specific interventions observed in the studies that were reviewed for this guideline.

Contraindications

Contraindications

- The product sheets of typical antipsychotic medications specify Parkinson's disease in the contraindications, warnings, and special precautions for use, because it can reduce the antiparkinson effects of levodopa, exacerbating the symptoms of the disease.
- Sildenafil is contraindicated in patients being treated with nitrates for cardiac coronary disease.

Qualifying Statements

Qualifying Statements

This clinical practice guideline (CPG) is an aid to decision-making in health care. The guidelines are not mandatory, nor do they take the place of the clinical judgement of healthcare staff.

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation

Clinical practice guidelines (CPGs) are tools to assist professionals and users to make decisions regarding the most appropriate healthcare treatment. To improve the implementation of a CPG, in other words, its introduction into the clinical environment, it is helpful to design a series of strategies aimed at overcoming possible barriers to adoption.

The plan for the implementation of this CPG for the management of patients with Parkinson's disease (PD) includes the following strategies:

- Presentation of the CPG by the healthcare authorities to the communication media
- Presentation of the CPG to the different national associations and societies for neurology, family and community medicine, physical therapy and medicine, pharmacy, nursing, physical therapy, occupational therapy, speech therapy, psychology, human nutrition and diet, etc.
- Presentation of the CPG to the pertinent regional associations
- Collaboration with scientific societies that have participated in the preparation of this CPG, to promote distribution
- Sending and distribution of the CPG to the different databases that collect information on CPGs, for evaluation and inclusion
- Contact with the Spanish Parkinson's Federation (FEP) and other associations of interested persons to present the guidelines to them.
- Free access to the different versions of the GPC at the GuíaSalud Web site .
- Distribution of information on the CPG at scientific activities (conferences, congresses, meetings) related to neurology, family and community medicine, physical therapy and medicine, pharmacy, nursing, physical therapy, occupational therapy, speech therapy, psychology, human nutrition and diet, etc.
- Information on the CPG in medical journals and magazines for the specialisations involved
- Publicising the existence and objectives of the CPG by means of mailing lists for professionals who would be potentially interested in it
- Translation of the complete version into English

A study of the barriers and facilitators in the implementation of the CPG is recommended, with interventions in the area of the healthcare professionals (skills, attitudes, opinions, motivation for change or individual characteristics), social context (patients and colleagues), factors related to the system (organization and structure, or economic measures), and aspects related to the CPG itself.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Working Group of the Clinical Practice Guideline for the Management of Patients with [trunc]. Clinical practice guideline for the management of patients with Parkinsonâ€™s disease. Madrid (Spain): Ministry of Health, Social Services and Equality; Institute of Health Sciences of Aragon;

2014. 159 p. [124 references]

Adaptation

Not applicable: The guideline is not adapted from another source.

Date Released

2014

Guideline Developer(s)

Aragon Institute for Health Sciences - State/Local Government Agency [Non-U.S.]

GuiaSalud - National Government Agency [Non-U.S.]

Ministry of Health (Spain) - National Government Agency [Non-U.S.]

Guideline Developer Comment

Corporate Collaborators

- Spanish Association of Physical Therapists (AEF)
- Spanish Association of Speech Therapy and Audiology (AELFA)
- Spanish Association of Neuropsychiatry (AEN)
- Spanish Association of Professional Occupational Therapists (APETO)
- Federation of Associations of Community Nursing and Primary Care (FAECAP)
- Spanish Parkinson's Federation (FEP)
- Spanish Foundation of Dieticians-Nutritionists (FEDN)
- Spanish Society of Primary Care Pharmacists (SEFAP)
- Spanish Society of Family and Community Medicine (SemFYC)
- Spanish Society of General and Family Physicians (SEMG)
- Spanish Society of Primary Care Physicians (SEMERGEN)
- Spanish Neurology Society (SEN)
- Spanish Psychiatry Society (SEP)
- Spanish Biological Psychiatry Society (SEPB)
- Spanish Society of Rehabilitation and Physical Medicine (SERMEF)

Members of these societies participated as authors, collaborating experts, or external reviewers of this clinical practice guideline (CPG).

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Guideline Committee

Working Group of the Clinical Practice Guideline for the Management of Patients with Parkinson's Disease

Composition of Group That Authored the Guideline

Working Group Members: Adrián Arés Luque, Doctor of Medicine, Neurology Specialist, León University Hospital, León; Eduard Baladia Rodríguez, Dietician-Nutritionist, Spanish Foundation of Dieticians-Nutritionists, Barcelona; Olga Bruna Rabassa, Neuropsychologist, Blanquerna Department of Psychology, Ramón Llull University, Barcelona; Inmaculada Calvo Muñoz, Physical Therapist, Altiplano Educational and Psycho-paedagogical Guidance Team, Jumilla, Murcia; Marcelo Chouza Insua, Physical Therapist, Department of Physical Therapy of the University of A Coruña, A Coruña; Alberto Frutos Pérez-Surio, Pharmacist, Specialist in Hospital Pharmacy, Institute of Health Sciences of Aragon, Zaragoza; Mª Victoria Hernández Jaras, Pharmacist, Specialist in Hospital Pharmacy and Primary Care Pharmaceuticals, Pharmacy Service SUMMA 112, Madrid; Luís Javier López del Val, Doctor of Medicine, Neurology Specialist, Lozano Blesa University Hospital, Zaragoza; Juan Ignacio Martín Sánchez, Doctor of Medicine, Specialist in Preventive Medicine and Public Health, Institute of Health Sciences of Aragon, Zaragoza; Maria Carmen Pilar Martínez Altarriba, Physician specialized in Family and Community Medicine, CAP Horta-Barcelona, Barcelona; Ana Novo Porca, Physical Therapist, Neurofis Centre of Neurological Physical Therapy, Ferrol, A Coruña; Luís Pintor Pérez, Doctor of Medicine, Specialist in Psychiatry, Clinical Hospital of Barcelona, Barcelona; Miguel Puyuelo Sanclemente, Psychologist and Speech Therapist, University of Zaragoza, Zaragoza; Raquel Terrén Bescos, Nurse, Nuestra Señora de Gracia Hospital, Zaragoza; Fernando Vázquez Sánchez, Doctor of Medicine, Neurology Specialist, Centre Hospitalier de Bigorre, Tarbes, Hautes Pyrénées, France, and Public Health (CIBER-ESP), Seville

Coordination: Alberto Frutos Pérez-Surio, Pharmacist, Specialist in Hospital Pharmacy, Institute of Health Sciences of Aragon, Zaragoza; Juan Ignacio Martín Sánchez, Doctor of Medicine, Specialist in Preventive Medicine and Public Health, Institute of Health Sciences of Aragon, Zaragoza

Other Collaborations

Documentation: María Pilar Blas Diez, Documentation Technician, Institute of Health Sciences of Aragon, Zaragoza

Design Information for Patients: Sofía Arguis Molina, Technician in Documentation and Information Systems, Institute of Health Sciences of Aragón, Zaragoza; María Gálvez Sierra, Sociologist, Director-General of the Spanish Parkinson's Federation, Madrid

Logistical and Administrative Support: María Esther García Pomar, Institute of Health Sciences of Aragon, Zaragoza

Revision of Information for Patients: María Yamina Fandos Falo, Zaragoza; Jonathan Giráldez Sánchez, Zaragoza

Expert Collaboration: Beatriz Álvarez Santafé, Nurse, Lozano Blesa University Hospital, Zaragoza; Enrique Arrieta Antón, Doctor of Medicine, Specialist in Family and Community Medicine, C. S. Segovia Rural, Segovia; Mª Jesús Calvo Til, Occupational Therapist, University of Zaragoza, Zaragoza; María Gálvez Sierra, Sociologist, Director-General of the Spanish Parkinson's Federation, Madrid; Eva López Valdés, Doctor of Medicine, Neurology Specialist, San Carlos Clinical Hospital, Madrid; Mario Páramo Fernández, Doctor of Medicine, Specialist in Psychiatry, Conxo Hospital Santiago de Compostela, A Coruña

External Review: Eva Pilar Chueca Miguel, Psychologist and Occupational Therapist, Parkinson's Association Aragón, Zaragoza; Rosario Luquin Piudo, Doctor of Medicine, Neurology Specialist, Consulting Neurologist at the University of Navarre Clinic, Pamplona; Juan Antonio Martín Jiménez, Doctor of Medicine, Specialist in Family and Community Medicine, Buenavista Health Centre (SESCAM), Toledo; María Carmen Martínez Garre, Doctor of Medicine, Specialist in Physical Medicine and Rehabilitation, Vall d'Hebron University Hospital, Barcelona; Mª Elena Martínez Rodríguez, Doctor of Medicine, Specialist in Physical Medicine and Rehabilitation, Ramón y Cajal University Hospital, Madrid; Juan Medrano Albéniz, Doctor of Medicine, Specialist in Psychiatry, Mental Health Network of Bizkaia, Portugalete, Vizcaya; Antonio Miguel Romeo, Physical Therapist, Dependence Evaluation Service of the Government of Aragón, Zaragoza; Pedro José Moreno Álvarez, Doctor of Medicine, Specialist in Family and Community Medicine, Director of the Clinical Management Unit at UGC La Rinconada, Sevilla; Mª del Pino Sanz Hernández, Nurse, Member of the Federation of Associations of Community Nursing and Primary Care, Zaragoza; Jorge Pla Vidal, Doctor of Medicine, Specialist in Psychiatry, University of Navarre Clinic, Department of Medical Psychology and Psychiatry, Pamplona; Armando Santo González, Doctor of Medicine, Specialist in Family and Community Medicine, C.S. Sangonera La Verde, Murcia; Jesús Seco Calvo, Doctor of Medicine, Specialist in Family and Community Medicine, Doctor of Medicine, Specialist in Physical Education and Sports Medicine, Physical Therapist, Institute of Biomedicine (IBIOMED), University of León

Financial Disclosures/Conflicts of Interest

All members of the Working Group, as well as those who have participated in the expert collaboration and external review, have made the declaration of interest as shown in Appendix 5 in the original guideline document.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available in English and Spanish from the GuíaSalud Web site.

Availability of Companion Documents

The following are available:

- Quick reference guides and summary versions are available from the GuíaSalud Web site.
- Working Group for CPG Updates. Updating clinical practice guidelines in the National Health System: methodology handbook. Madrid (Spain): National Health System Quality Plan of the Spanish Ministry of Health and Social Policy; Aragon Institute for Health Sciences (IACS); 2009. 67 p. (Clinical Practice Guidelines in the National Health System: IACS; no. 2007/02-01). Available from the GuíaSalud Web site.
- The Spanish version of the guideline is also available via a mobile application from the GuiaSalud Web site (http://portal.guiasalud.es/web/guest/app).

Patient Resources

Patient information can be found in Annex 2 of the original guideline document. A Spanish version is also available from the GuíaSalud Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on March 15, 2017. The information was verified by the guideline developer on April 10, 2017.

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